REMARKS/ARGUMENTS

Claims 1-13 were examined on the merit in the non-final Office action mailed February 2, 2008. Claims 1-13 have been canceled. With this Amendment, Claims 1-13 have been replaced with newly added claims 73-81. Upon the entry of this amendment, claims 14-81 are pending. Support for the amendment can be found in the present application. Accordingly, no question of new matter should arise, and entry of this amendment is respectfully requested.

Claims 14-81 are pending in the application. Claims 14-72 have been withdrawn from consideration by the examiner as drawn to the non-elected invention. Applicants specifically reserve the right to file one or more divisional applications to the non-elected subject matter.

By the above amendment, Applicants have rewritten claims 1-13 as newly presented claims 73-81 to more particularly and distinctly define the invention so as to overcome the technical rejections and to define the invention patentably over the prior art.

In the most recent Office action mailed on February 7, 2008, the Examiner has objected to claims 7, 10 and 11. In addition, the Examiner has rejected claims 7 and 8 Under 35 USC 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the same Office action mailed February 7, 2008, the Examiner has rejected claims 1-13 and 23-28 under 35 USC 103(a). The applicants submits the following remarks to address the Examiner's objections and rejections which taken in combination with the amendments presented herewith attempt to address each of the Examiner's concerns.

The Objection And the Claims Rejection under § 112

The present amendments address and avoid each of the Examiner's objections as

well as the issues raised by the rejection under 35 U.S.C. 112, second paragraph. Accordingly Applicants submit that claims do comply with § 112 and therefore request withdrawal of the object and the rejection.

Rejection under 35 USC 103(a):

The examiner has rejected claims 1-13 under 35 U.S.C 103 (a) as being unpatentable over Whitcomb (USPN 6011049 hereafter '049) in view of Pearson et al. (USPN 2003/0078269 hereafter '269).

The Examiner contends that Whitcomb discloses all of the limitations of claims 1-13 (Office Action, pages 5-7) with the exception of the teaching on the glycemic regulatory composition comprising a glitazone, a biguanide and a sulfonylurea where at least one of two of the components are released at a sustained and/or rapid rate ((Office Action, page 6, paragraph number 1). The Examiner also contends that Pearson et al. discloses these limitations that are not present in Whitcomb.

Applicants respectfully traverse this rejection and, to the extent they are maintained with respect to the claims as amended herein, request reconsideration and withdrawal of the rejections.

Initially, it is noted that the Office action (through the Examiner) has not identified where in Whitcomb and Pearson et al. the alleged teaching is to be found on all of the limitations of Claims 1-13. Still further, Applicants have carefully reviewed the remainder of patents to Whitcomb and Pearson et al, and find no teaching of all of the limitations of claims 1-13. Thus, for at least this reason, Whitcomb and Pearson et al., cannot make claims 1-13 obvious. Neither Whitcomb alone or in combination with Pearson et al, discloses an oral delivery system comprising a combination of

d) a slow release component comprising biguanide and a hydrophilic and/or at least one or more hydrophobic polymers and/or at least one or more hydrophobic materials,

e) a slow release or immediate release component comprising sulfonylurea and for slow release, a hydrophilic and/or at least one or more hydrophobic polymers and/or at least one or more hydrophobic materials,

f) an immediate release component comprising glitazone

wherein the delivery system is a fixed dose combination for the treatment of diabetes and its associated disorders.

Furthermore, applicants would like to bring to the attention of the Examiner towards the fact that Whitcomb merely discloses combinations for diabetes containing a sulfonylurea, biguanide, and glitazone. All the components are given as immediate release components. On the other hand, Pearson et al. merely gives a broad view that composition of the Pearson can be designed to give immediate release, or sustained release and broadly mentions about microspheres, liposomes, porous beads etc. Pearson does not exemplify any thing about the specific type of delivery system, which the instant application claims. There are no examples mentioned in Pearson, which exemplifies such delivery system. Further, Pearson does not teach or mentions about the slow release of biguanide or sulfonylurea specifically. It altogether gives a general disclosure and definition of terms controlled release, sustained release or timed release. It gives additional broad disclosure about targeted delivery or site-specific delivery. Nowhere in the application, Pearson mentions about the use of three actives biguanides, glitazones and sulfonylureas through a specific delivery mechanism and that too in a fixed dose combination. In fact, Pearson is more related to enhancement of glycemic control through use of certain other agents like cofactors, ions, amino acids etc in combination with antidiabetics.

Applicants want to highlight that subject matter claimed in instant application is related to specific delivery system in a fixed dose combination, wherein release of three different class of drugs having limited window of absorption in a combination is controlled or tailored in such a way so as to provide a dosage form that inherently has a prolonged gastric residence time. Such a delivery system results in improvement of glycemic control in diabetic patients in much better way coupled with adjustment of

dosage regimen wherein there is dose reduction for some therapeutic components in combination.

Applicants would like to bring to the attention of the Examiner that its very difficult to achieve the release of three active agents belonging to different classes having limited absorption window and that too in a single combination dosage form as release of one drug is drastically effected by the presence of the other. The delivery system of the instant application provides for slow release with minimal inter-patient variability in pharmacokinetic parameters. So, the distinguishing feature is the specific type of delivery system and not a mere combination or simple controlled release because it is very difficult to tailor the profile of altogether different categories of drug with limited absorption window and that too in a single dosage form which is totally new.

Furthermore, neither Whitcomb and/or Pearson et al., patent(s) teach or motivate one of ordinary skilled in the art to provide an oral delivery system comprising a combination of a slow release component comprising biguanide, a slow release or immediate release component comprising sulfonylurea and an immediate release component comprising glitazone. Hence the invention as claimed in our application is a significant technological advancement over the cited prior art.

As noted above that the Office Action fails to specifically address even the expressly recited features of the pending independent and dependent claims. Under the Office's policy of compact prosecution, each claim should be reviewed for compliance with every statutory requirement for patentability in the initial review of the application. (MPEP §707.07(g)). It is submitted that the present application is not sufficiently informal, does not present an undue multiplicity of claims, or exhibit a misjoinder of inventions, so as to reasonably preclude a complete action on the merits. Thus, it is submitted that the Office's failure constitutes a failure to expeditiously provide the information necessary to resolve issues related to patentability that prevents the Applicant from, for example, presenting appropriate patentability arguments and/or rebuttal

evidence. (See The Official Gazette Notice of November 7, 2003). Additionally, it is submitted that the Office's failure needlessly encourages piecemeal prosecution, which is to be avoided as much as possible. (MPEP §707.07(g)). Accordingly, in the event that the Office maintains the rejection of any of the independent and/or dependent claims, Applicant respectfully requests, in the interests of compact prosecution, that the Office apply art against each feature of each rejected independent and dependent claims, on the record, and with specificity sufficient to support a prima facie case of obviousness.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

It is well known that in order for any prior-art references themselves to be validly combined for use in a prior-art § 103 rejection, *the references themselves* (or some other prior art) must suggest that they be combined. E.g., as was stated in In re Sernaker, 217 U.S.P.Q. 1, 6 (C.A.F.C. 1983):

"[P]rior art references in combination do not make an invention obvious unless something in the prior art references would suggest the advantages to be derived from combining their teachings." That the suggestion to combine the references should not come from applicant was forcefully stated in Orthopedic Equipment Co. v. United States , 217 U.S.P.Q. 193, 199 (C.A.F.C. 1983):

"It is wrong to use the patent in suit [here the patent application] as a guide through the maze of prior art references, combining the right references in the right way to achieve the result of the claims in suit [here the claims pending]. Monday morning quarterbacking is quite improper when resolving the question of nonobviousness in a court of law [here the PTO]." As was further stated in Uniroyal, Inc. v. Rudkin-Wiley Corp., 5 U.S.P.Q.2d 1434 (C.A.F.C. 1988), "[w]here prior-art references require selective combination by the court to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself ... *Something in the prior art must suggest the desirability and thus the obviousness*

of making the combination." [Emphasis supplied.]

In line with these decisions, the Board stated in Ex parte Levengood, 28 U.S.P.Q.2d 1300 (P.T.O.B.A.&I. 1993):

"In order to establish a *prima facie* case of obviousness, it is necessary for the examiner to present *evidence*, preferably in the form of some teaching, suggestion, incentive or inference in the applied prior art, or in the form of generally available knowledge, that one having ordinary skill in the art *would have been led* to combine the relevant teachings of the, applied references in the proposed manner to arrive at the claimed invention. ...

That which is within the capabilities of one skilled in the art is not synonymous with obviousness. ... That one can *reconstruct* and/or explain the theoretical mechanism of an invention by means of logic and sound scientific reasoning does not afford the basis for an obviousness conclusion unless that logic and reasoning also supplies sufficient impetus to have led one of the ordinary skill in the art to combine the teachings of the references to make the claimed invention.... Our reviewing courts have often advised the Patent and Trademark Office that it can satisfy the burden of establishing a *prima facie* case of obviousness only by showing some objective teaching in either the prior art, or knowledge generally available to one of ordinary skill in the art, that 'would lead' that individual 'to combine the relevant teachings of the references.' ... Accordingly, an examiner cannot establish obviousness by locating references which describe various aspects of a patent applicant's invention without also providing evidence of the motivating force which would impel one skilled in the art to do what the patent applicant has done."

In the present case, there is no reason given in the last Office action to support the proposed combination. However the fact that both references teach biguanide, sulfonylurea and glitazone is not sufficient to gratuitously and selectively suggest that the one would be led to substitute parts of one reference for a part of another reference in order to meet applicants' novel claimed combination.

The references relied upon fail to provide an adequate basis in evidence to support the Examiner's initial conclusion of obviousness. In short there must be more than merely establishing that the individual components exist in the prior art. There must be something , found in the prior art which would have suggested , led or motivated one skilled in this art to bring those individual components together in the manner presently claimed. The present rejection lacks this aspect.

Applicants respectfully request, if the claims are again rejected upon any combination of references, that the Examiner include an explanation, in accordance with M.P.E.P. § 706.02. Ex parte Clapp, 27 U.S.P.Q. 972 (P.O.B.A. 1985), and Ex parte Levengood, supra, a "factual basis to support his conclusion that would have been obvious" to make the combination.

It is respectfully requested that this rejection be reconsider and withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance and notification to that effect is earnestly requested. If desired, the examiner is invited to conduct a telephone conference to expedite the prosecution of the subject application. In such a case, the examiner is invited to call the undersigned attorney.

Should any official at the United States Patent and Trademark Office deem that any further action by the Applicants or Applicants' undersigned representative is desirable and/or necessary, the official is invited to telephone the undersigned at the number set forth below.

The Commissioner is herby authorized to charge any fees which may be required regarding this application under 37 CFR §§ 1.16-1.17 or credit any overpayment, to deposit account No. 503321. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, or otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 503321.

Respectfully submitted,

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